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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/598,606	12/14/2006	Seppo Sarna	0933-0284PUS1	7736

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EXAMINER	
BORIN, MICHAEL L	

ART UNIT	PAPER NUMBER
1631	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/598,606	SARNA ET AL.	
	Examiner	Art Unit	
	Michael Borin	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) *13-15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/04/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

As a preliminary matter, Examiner acknowledges that claims of Preliminary Amendment, rather than original claims should have been addressed in the restriction requirement. Claims 1-15 are pending and are being addressed as follows.

Response to restriction requirement filed is acknowledged. Applicant elected, with traverse, Group I, claims 1-12. Applicant argues that the cited reference of Väänänen et al does not teach the special technical feature of the present invention as, although measuring "markers" is indeed taught in the reference, it does not teach "dynamic relationship between the measured amount of the markers and the diseases". Examiner disagrees. First, the claims are not directed to a dynamic relationship between the measured amount of the markers and the diseases; second, high predictive values of correlation between levels of markers and state of mucosa demonstrated in the reference suggest using them for determining probability of for gastric mucosa to belong to a certain mucosa type based on thus determined markers levels (see art rejection below). The lack of unity requirement is still deemed proper and is therefore made FINAL. Claims 13-15 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected groups. Cancellation of claims 13-15 is requested.

As per election of species requirement, applicant's argument are deemed persuasive and the election f species requirement is withdrawn.

Priority

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d).

Information Disclosure Statement

Applicants' Information Disclosure Statement filed 12/04/2006 has been received and entered into the application. Accordingly, as reflected by the attached completed copies of forms PTO-1449, the cited references have been considered.

Abstract

The abstract of the disclosure is objected to because an abstract on a separate sheet is required . Correction is required.

Claim Rejections - 35 U.S.C. § 101

The following is a quotation of the 35 U.S.C. § 101:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

Claims 1-12 are ejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The instant claims are drawn to a computational process of correlating the presence of markers, namely pepsinogen I, gastrin-17, and Helicobacter pylori marker with a state of gastric mucosa.

The claims do not recite any physical transformation step, nor they recite a tie to another category of invention.

To qualify as a statutory process, the claims should positively recite the other statutory class (the thing or product) to which it is tied, for example by identifying the apparatus that accomplishes the method steps, or positively recite the subject mater that is being transformed, for example by identifying the material that is being changed to a different state or thing. In the instant case, claims do not recite any physical transformation step. Further, there is no step in the claims that recites a tie to another category of invention. Therefore, the claims are drawn to non-statutory subject mater for failing to recite a step that ties the method to another category of invention.

The "measuring" step to detect presence or amount of markers is considered as a nominal data gathering step that merely provides the raw materials, the information, used in "correlating" levels of the markers with a state of gastric mucosa. Nominal data gathering or post solution activity steps in the claimed subject matter are not considered sufficient to convert a process that otherwise recites only mental steps into statutory subject matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Väänänen et al (European Journal of Gastroenterology & Hepatology, 2003, 15(8), 885-891) or Suovaniemi (US 2004003837; now US Patent 7,358,062) in view of García-Fernándes Nephron 2002;92:97-104) and Ashton et al. (US 6,950,544).

The instant claims are drawn to method for assessing or predicting the state of the gastric mucosa in a subject by determining the probability for the gastric mucosa belonging to at least one gastric mucosa class, the method comprising

a) measuring, from a sample of said subject,

- the pepsinogen I (PGI) and

- gastrin-17 (G-17) analyte concentrations, as well as
- determining the presence or concentration of a marker for Helicobacter pylori

b) entering the data in a data processing system to determine the probability for the gastric mucosa belonging to the at least one gastric mucosa class based on

- the data entered, as well as
- on predefined clinical data in the database,

the information so generated by the data processing system being indicative of the state of the gastric mucosa in said subject

Väänänen et al teach measuring in a subject

- serum levels of gastrin-17 (S-G-17),
- pepsinogen I (S-PGI), and
- assaying *Helicobacter pylori* antibodies

Gastrin and pepsinogen levels were compared with clinical history of patients. S-G-17_{prand} (and S-G-17_{fast}) and S-PGI levels decreased with increasing grade of atrophy of the antrum or corpus, respectively. S-G-17_{prand} levels were significantly lower in patients with advanced (moderate or severe) atrophic antral *H. pylori* gastritis than in those with non-atrophic *H. pylori* gastritis. All patients with a resected antrum demonstrated S-G-17_{prand} levels that were almost undetectable.

Similarly, comparing *H. pylori*-positive antibody assay results with clinical history demonstrated correlation of *H. pylori* assay results with atrophic antral gastritis Similarly, S-PGI levels were significantly lower in patients with advanced corpus atrophy than in those without.

The sensitivity and specificity of the blood test panel in delineation of patients with advanced atrophic gastritis (either in the antrum or the corpus, or both) were 83% and 95%, respectively. The predictive values of the positive and negative test results were 75% and 97%, respectively.

Thus, the reference teaches measuring the said markers and determining the probability for the gastric mucosa belonging to advanced atrophic gastritis, either in the antrum or the corpus or both, based on the results of the measurements combined with clinical data .

Suovaniemi (US 20040038376; now US Patent 7,358,062) teaches a method for assessing the condition of the gastric mucosa, especially for diagnosing mucosal gastric changes, such as atrophic gastritis, in a subject, by assaying the analytes

pepsinogen I (PGI),

gastrin and

a marker for Helicobacter pylori infection,

the method comprising measuring from a sample of said subject the pepsinogen I and gastrin concentration, and, in addition, determining the concentration or presence of a marker for Helicobacter pylori, entering the data so obtained for said analytes in a data processing means comprising an operating system, means for transceiving and processing data, said data processing means being adapted to perform the steps of comparing a measured concentration value for an analyte to a predetermined cut-off value for said analyte, to obtain a combination of comparison results which is specific

for the subject tested, and generating information in response to the said combination of comparison results.

Further, with respect to claim 10, Suovaniemi et al teach further measuring pepsinogen II (PGII), forming a PGI/PGII ratio and entering said PGI/PGII ratio into said data processing system (see claim 5).

The references do not teach determining probability for the gastric mucosa to belong to atrophic gastritis tissue.

However, high level of predictive values correlating levels of the markers discussed above with the presence or absence of atrophic gastritis tissue make it obvious that measuring the amounts/presence of these markers can be used to determine probability that a tissue belongs to a particular condition of interest.

Regression analysis of clinical data is routinely used to determine probabilities of events or occurrences of interest. As an example, García-Fernánde teaches using prediction model based on applying of univariate and multivariate logistic regressions of clinical data comprising levels of PAI-1 antigen, t-PA antigen, and prothrombin fragment to determine probability of death outcome.

Furthermore, it is known that when a plurality of parameters (markers) are known, probability of a tissue to belong to a certain type can be determined using "probability maps". See US 6950544 (Ashton et al) , for example, wherein the probability map represents a probability that each of the plurality of structures is found in any given image element. Although US 6950544 is directed to use of image information – as opposed to marker presence in the instant invention – it would be obvious to apply the same approach to gastrin and pepsinogen and H. pilori data. Consequently, it

would be obvious to use the system for automated probability determination comprising operation system, database and suitably programmed processor, such as system taught in US 6950544 (see claim 46), to determine probability of predicting a state of gastric mucosa using markers discussed in Väänänen et al.

Further, with regard to using a "data processing system", as instructed by MPEP, chapter 2106 II, merely using a computer to automate a known process does not by itself impart nonobviousness to the invention. The use of particular mathematical or computerized means would have accomplished the same result would be an obvious mathematical and/or computational way of determining and presentation of results.

With respect to dependent claims 2-9,11,12 if there are any differences between Applicant's claimed method and that of the prior art, the differences would be appear minor in nature. The nature of the problem to be solved – generating and using predictive clinical data - would lead inventors to look at references relating to possible factors known to determine selection of appropriate markers, data acquisition, analysis, presentation as well as future use of the predictive model. One of ordinary skill in the art would have been motivated to combine all known factors with no change in their respective functions, and the combination would have yielded nothing more than predictable results.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 66-69,72-76,78-107 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-26 of U.S. Patent No. 7,358,062 in view of García-Fernándes Nephron 2002;92:97-104) and Ashton et al. (US 6,950,544).

US Patent 7,358,062 teaches a method for assessing the condition of the gastric mucosa, especially for diagnosing mucosal gastric changes, such as atrophic gastritis, in a subject, by assaying the analytes pepsinogen I (PGI), gastrin and a marker for Helicobacter pylori infection, the method comprising measuring from a sample of said subject the pepsinogen I and gastrin concentration, and, in addition, determining the concentration or presence of a marker for Helicobacter pylori, entering the data so obtained for said analytes in a data processing means comprising an operating system, means for transceiving and processing data, said data processing means being adapted to perform the steps of comparing a measured concentration value for an analyte to a predetermined cut-off value for said analyte, to obtain a combination of comparison results which is specific for the subject tested, and generating information in response to the said combination of comparison results.

Further, with respect to claim 10, Suovaniemi et al teach further measuring pepsinogen II (PGII), forming a PGI/PGII ratio and entering said PGI/PGII ratio into said data processing system (see claim 5).

US Patent 7,358,062 does not teach determining probability for the gastric mucosa to belong to atrophic gastritis tissue.

However, high level of predictive values correlating levels of the markers discussed above with the presence or absence of atrophic gastritis tissue make it obvious that measuring the amounts/presence of these markers can be used to determine probability that a tissue belongs to a particular condition of interest.

Regression analysis of clinical data is routinely used to determine probabilities of events or occurrences of interest. As an example, García-Fernánde teaches using

prediction model based on applying of univariate and multivariate logistic regressions of clinical data comprising levels of PAI-1 antigen, t-PA antigen, and prothrombin fragment to determine probability of death outcome.

Furthermore, it is known that when a plurality of parameters (markers) are known, probability of a tissue to belong to a certain type can be determined using "probability maps". See US 6950544 (Ashton et al) , for example, wherein the probability map represents a probability that each of the plurality of structures is found in any given image element. Although US 6950544 is directed to use of image information – as opposed to marker presence in the instant invention – it would be obvious to apply the same approach to gastrin and pepsinogen and H. pilori data. Consequently, it would be obvious to use the system for automated probability determination comprising operation system, database and suitably programmed processor, such as system taught in US 6950544 (see claim 46), to determine probability of predicting a state of gastric mucosa using markers discussed in Väänänen et al.

Prior art made of record

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure

WO 96/15456 a method for determining detecting atrophy of the corpus or antrum area of the stomach, or atrophy of the mucosa of the stomach by measuring

concentration of the analytes pepsinogen I, and gastrin-17 from a serum sample of a subject; the said tests may be combined with a test for Helicobacter pylori antibodies. The determined concentration values are then compared to a cut-off value and a reference value for each analyte. A serum pepsinogen I concentration below the cut-off value for pepsinogen I in combination with a gastrin-17 concentration value above the upper reference limit indicates severe atrophy of the corpus area of the stomach. A serum gastrin-17 level below the cut-off value for gastrin-17 in combination with a pepsinogen I value above the cut-off value for pepsinogen I on the other hand indicates atrophy of the antrum area of the stomach. In case the serum pepsinogen I is below the cut-off value for pepsinogen I, and the gastrin-17 level is at the lower limit of its reference value, this is an indication of severe atrophy in the whole stomach, i.e. of atrophic pangastritis.

Valle et al teach a method of assessing the condition of the gastric mucosa through measuring pepsinogen, a Helicobacter pylori marker and gastrin in a subjects' sample and utilizes a computer for data analysis,

Harkonen (US Pat. 6,696,262) and Sipponen (Scandinavian journal of gastroenterology, (2002 Jul) Vol.37, No. 7, pp. 785-791) show measurement of PGI, Gastrin-17 and a Helicobacter marker

Schlemper et al (1995) is cited to show the measurement of gastrin, pepsinogen I, pepsinogen II and PGI/PGII (A/C) ratio as a measurement of changes in the mucosa (see Figure 1, page 199)

Conclusion.

No claims are allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Borin whose telephone number is (571) 272-0713. The examiner can normally be reached on 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached on (571) 272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael Borin, Ph.D./
Primary Examiner, Art Unit 1631

mlb